Prenatal Diagnosis of a 4.9-Mb Deletion of 10q11.21 → q11.23 by Array Comparative Genomic Hybridization

Chih-Ping Chen[1,2,3,4,5,6]*, Yi-Ning Su[7], Schu-Rern Chern[2], Fuu-Jen Tsai[4,8,9], Chin-Yuan Hsu[1], Chen-Chi Lee[1], Wayseen Wang[2,10]

Departments of [1]Obstetrics and Gynecology and [2]Medical Research, Mackay Memorial Hospital, Taipei, [3]Department of Biotechnology, Asia University, [4]School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, [5]Institute of Clinical and Community Health Nursing, National Yang-Ming University, [6]Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, [7]Department of Medical Genetics, National Taiwan University Hospital, Taipei, Departments of [8]Medical Genetics and [9]Medical Research, China Medical University Hospital, Taichung, and [10]Department of Bioengineering, Tatung University, Taipei, Taiwan.

A 32-year-old primigravid woman was referred to Mackay Memorial Hospital at 22 weeks of gestation for confirmation of a *de novo* interstitial deletion of chromosome 10q in the fetus. The woman and her husband were healthy, and there was no family history of congenital malformations. Detailed high-resolution ultrasound revealed a singleton fetus consistent with 22 weeks of gestation, with no gross abnormalities. The woman had undergone elective amniocentesis at 18 weeks of gestation because of maternal anxiety. Conventional cytogenetic analysis revealed a 46,XY karyotype. However, elective bacterial artificial chromosome-based array comparative genomic hybridization (aCGH) using cultured amniocytes from 10 mL amniotic fluid revealed a 4.9-Mb deletion of 10q11.21 → q11.23 or arr cgh 10q11.21q11.23 (RP11-23H7 → RP11-590C17) × 1 (Figure 1). aCGH analysis of parental blood revealed no such deletion in the parents. Repeat amniocentesis was performed at 22 weeks of gestation, and 40 mL of amniotic fluid was aspirated. aCGH was performed using uncultured amniocytes from 20 mL, while the remaining 20 mL was used for conventional cytogenetic analysis. Conventional cytogenetic analysis revealed a 46,XY,del(10)(q11.21q11.23) karyotype (Figure 2). Oligonucleotide-based aCGH demonstrated partial monosomy 10q [arr cgh 10q11.21q11.23 (45,946,150-50,945,014 bp) × 1] with a deletion of 4,998,865 bp (Figure 3). The parents opted to terminate the pregnancy at 24 weeks of gestation, and an 820-g fetus with facial dysmorphism, including hypotelorism, micrognathia and large, low-set ears, was delivered.

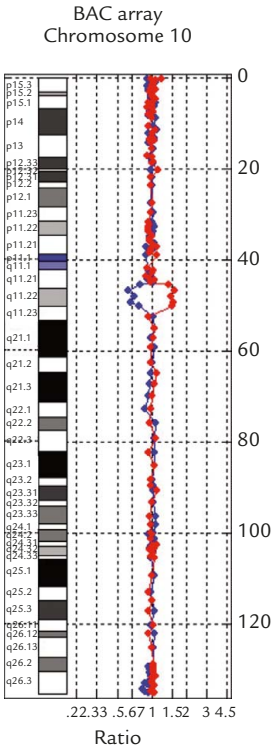

Figure 1. Bacterial artificial chromosome (BAC)-based array comparative genomic hybridization analysis using CMDX (CMDX, Irvine, CA, USA) BAC array comparative genomic hybridization CA3000 chips showed an interstitial deletion of proximal 10q [arr cgh 10q11.21q11.23 (RP11-23H7 → RP11-590C17) × 1].

*Correspondence to: Dr Chih-Ping Chen, Department of Obstetrics and Gynecology, Mackay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei, Taiwan.
E-mail: cpc_mmh@yahoo.com
Accepted: November 13, 2009

We have presented a case of prenatal diagnosis and molecular characterization of a *de novo* interstitial deletion of proximal 10q. Prenatal diagnosis of a deletion in the proximal region of the long arm of chromosome 10 has not been previously described. The present case had minor facial dysmorphism but no sonographically recognizable structural defects. This represents the shortest reported deletion within the chromosome segment 10q11.2. Only two previous cases of del(10)(q11.2 → q21) have been previously reported, both associated with minor dysmorphism, mental retardation and developmental delay. Ray et al [1] reported a 1-year-old boy with a 46,XY,del(10)(q11q21) karyotype, mental retardation, significant developmental delay, plagiocephaly, torticollis, limitation of extension at the knees, hips and elbows, mild hypotonia, mild micrognathia, an asymmetric face, telecanthus, a large mouth, and large, low-set ears. Holden and MacDonald [2] reported a 9-year-old girl with a 46,XX,del(10)(q11.2q21) karyotype, cleft palate, bilateral ptosis, low-set ears, developmental delay, mild hypotonia, deficit in language function, mental retardation, and seizures. Common findings in the reported cases with del(10)(q11.2 → q21) included mental retardation, developmental delay, mild hypotonia, sparse, fine hair, and dry skin [1,2]. In this regard, prenatal diagnosis of a deletion of proximal 10q should alert physicians to the possible association with mental retardation and developmental delay, even though it is associated with minor anomalies.

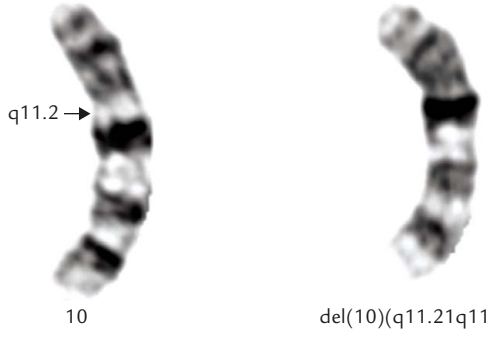

Figure 2. Partial karyotype showing del(10)(q11.21q11.23). Arrow indicates the region of 10q11.2.

The present case was associated with a 4.9-Mb deletion, which is very close to the detection limit of conventional cytogenetics at the regular banding level. We previously reported prenatal diagnosis of a 22q11.2 microdeletion using cultured amniocytes [3] and an unbalanced translocation using uncultured amniocytes [4]. In this report, we further demonstrated the use of aCGH as a powerful tool for the diagnosis of subtle chromosome abnormalities that are undetectable by regular conventional cytogenetic analysis. aCGH using cultured or uncultured amniocytes has been successfully applied for the prenatal diagnosis of chromosome abnormalities. It has the advantage of providing a rapid, genome-wide study without the need for cell culture.

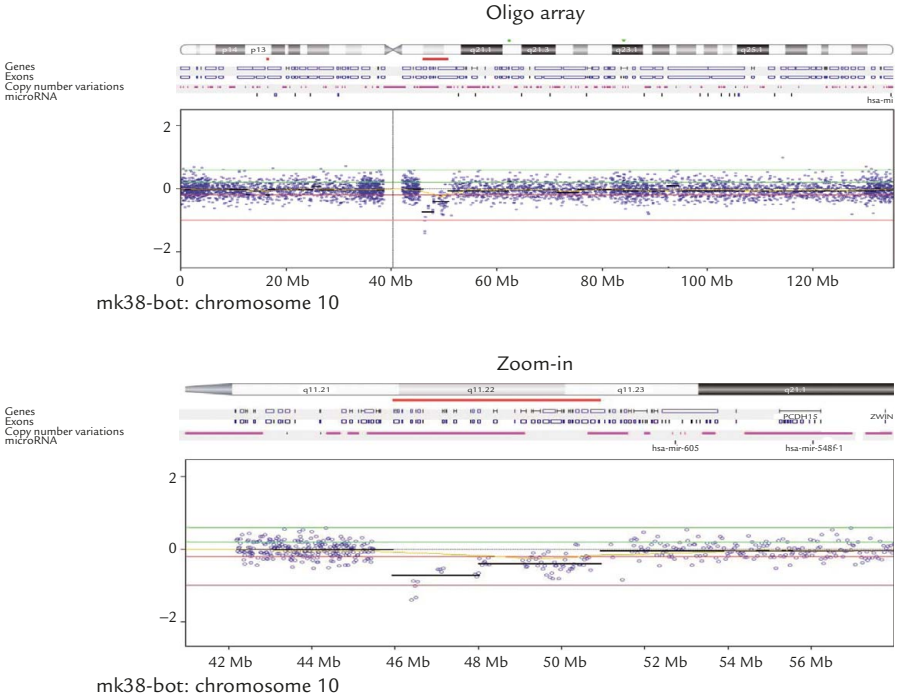

Figure 3. Oligonucleotide-based array comparative genomic hybridization analysis using Oligo HD Scan (CMDX, Irvine, CA, USA) showed a 4.9-Mb deletion in 10q11.21 → q11.23 [arr cgh 10q11.21q11.23 (45,946,150-50,945,014 bp) × 1] with a deletion of 4,998,865 bp.

aCGH is able to detect chromosome deletions and duplications of less than 100 kb, whereas conventional cytogenetic analysis can only detect those larger than 5–6 Mb at the 500-band level [5]. We suggest that aCGH using cultured or uncultured amniocytes is a useful adjunct to conventional cytogenetic analysis for the prenatal diagnosis of subtle chromosome abnormalities following amniocentesis.

Acknowledgments

This work was supported by research grants NSC-96-2314-B-195-008-MY3 and NSC-97-2314-B-195-006-MY3 from the National Science Council, and MMH-E-98004 from Mackay Memorial Hospital, Taipei, Taiwan.

References

1. Ray M, Hunter AGW, Josifek K. Interstitial deletion of the long arm of chromosome 10. *Ann Genet* 1980;23:103–4.
2. Holden JJA, MacDonald EA. Brief clinical report: interstitial deletion of the long arm of chromosome 10: del(10)(q11.2q21). *Am J Med Genet* 1985;20:245–8.
3. Chen CP, Su YN, Chang TY, et al. 22q11.2 microdeletion in a fetus with double-outlet right ventricle, pulmonary stenosis and a ventricular septal defect: prenatal diagnosis by array comparative genomic hybridization. *Taiwan J Obstet Gynecol* 2009;48:437–40.
4. Chen CP, Su YN, Tsai FJ, et al. Terminal 2q deletion and distal 15q duplication: prenatal diagnosis by array comparative genomic hybridization using uncultured amniocytes. *Taiwan J Obstet Gynecol* 2009;48:441–5.
5. Breman AM, Bi WM, Cheung SW. Prenatal diagnosis by array-based comparative genomic hybridization in the clinical laboratory setting. *Beijing Da Xue Xue Bao* 2009;41:500–4.